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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,318	11/16/1999	PATRICIA L. CONKLIN	BTI-41	4166

20808 7590 12/31/2003

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,318	CONKLIN ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 November 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Notice of Non-Response amendment mailed 13 November 2003 was sent inadvertently and is thus WITHDRAWN.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The objection to claims 2-8, 10-15 and 17-22 because of informalities is WITHDRAWN in light of Applicant's amendments to the claims.

4. It is noted that in paragraph 2 of the Declaration of Dr. Patricia Conklin, filed 17 September 2003, there are blank lines where dates should be.

Claim Objections

5. Claims 6-7, 13-14 and 20-21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. If transformation of a plants with a nucleic acid encoding phosphoglucose isomerase, phosphomannomutase, GDP-mannose pyrophosphorylase (GMPase), or GDP-D-mannose-3,5-epimerase increases the levels of levels of vitamin C in a plant and increasing the resistance to environmental stress, this would be inherent features of the plants of parent claims 1 and 9 and an inherent result of the method of parent claims 16. Thus, claims 6-7, 13-14 and 20-21 fail to further limit claims 1, 9 and 16.

Claim Rejections - 35 USC § 112

6. Claims 1-22 and 24-26 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is modified from the rejection set forth in the Office action mailed 17 June 2003. Applicant's arguments and the Declaration of Dr. Patricia Conklin, both filed 17 September 2003, have been fully considered but they are not persuasive.

The claims are broadly drawn to a method of increasing the levels of vitamin C in a plant and increasing the resistance to environmental stress by expression a nucleic acid that encodes an enzyme in a plant biosynthetic pathway, wherein the enzyme is phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-D-mannose-3,5-epimerase, and plants thereby obtained.

The instant specification only provides guidance for EMS mutagenesis of *Arabidopsis* to produce two mutants, named *vtc*, that are deficient in AsA production (pg 7-9); testing the mutants for loss of conversion from mannose to ascorbic acid (pg 9-10); AFLP mapping of the *vtc* loci - *vtc1* maps within a published BAC that has as one of its open reading frames a putative mannose-1-phosphate guanyltransferase, aka GDP-mannose pyrophosphorylase, and for which a partial sequence has been published in GenBank as Accession No. T46645; this sequence is mutated in *vtc1-1* and *vtc1-2* (pg 10-12); measuring GDP-mannose pyrophosphorylase activity in *vtc1* mutants (pg 12-13); and complementation of the *vtc1-1* mutant with a 3.4 kb subfragment from the BAC clone that has the GDP-mannose pyrophosphorylase gene (pg 13-17).

The instant specification fails to provide guidance for the sequence of the full-length gene encoding GMPase, and thus provide guidance for wild-type plants transformed with the GMPase gene and methods of making stress resistant plants by transformation with a nucleic acid

encoding the GMPase gene. The specification also fails to provide guidance for nucleic acids encoding phosphoglucose isomerase, phosphomannomutase, or GDP-D-mannose-3,5-epimerase, and thus provide guidance for wild-type plants transformed with the GMPase gene and methods of making stress resistant plants by transformation with a nucleic acid encoding any of these enzymes.

The specification does not teach the sequence of full-length Arabidopsis GMPase gene. GenBank Accession No. T46645 is only 510 nucleotides long and only encodes a protein of 83 amino acids, as shown below:

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T46645

ATTTTGCCAACGAACGTTCTTTCTTCTTAATCACAGCNCAGCCTGACGCAACCGCTCAGGCTGATCTN
TTCCAATTTACAGCCATTTCCCAGCTCAGATCTCTGATCCGGTGAGATCTCTCTCAAGGAAAAGGAGT

TAGAGCATCATCAAGATGAAGGCACTCATTCTTGTTGGAGGCTTCGGCACTCGCTTGAGACCATTGAC
                MetLysAlaLeuIleLeuValGlyGlyPheGlyThrArgLeuArgProLeuTh

TCTCAGTTTCCCAAAGCCCCTTGTTGATTTTNCTAATAAACCCATGATCCTTCATCAGATAGAGGCTC
rLeuSerPheProLysProLeuValAspPheXXXAsnLysProMetIleLeuHisGlnIleGluAlaL

TTAAGGCAGTTGGAGTTGATGAAGTGGTTTTGGCCATCAATTATCAGCCAGAGGTGATGCTGAACTTC
euLysAlaValGlyValAspGluValValLeuAlaIleAsnTyrGlnProGluValMetLeuAsnPhe


TTGAAGGACTTTNAGACCAAGCTGGAAATCAAAATCACTTGCTCACAAGAGCCGAGCNACTAGGTACC
LeuLysAspPheXXXThrLysLeuGluIleLysIleThrCysSerGlnGluProSerXXXstp

GCTGGTCCTTGGTTTANNGGGNGCAAATTGNTTTATGGACCTGNGNGCCCTTTTTGTTTTAAAAGNNA
TGANTAAGGGGNCCCNNTAAANAANCTTNGGGTT
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The specification on pg 11, lines 3-15 states that the protein encoded by T46645 has 59% identity to the mannose-1-phosphatse guanyltransferase from *Saccharomyces cerevisiae*. However, this enzyme from yeast is 361 amino acids long (Schultz et al, 2002, GenBank Accession No. P41940). T46645 only encodes a protein that is about 23% of the length of the yeast protein sequence. Thus, it is clear that T46645 does not encode a full-length enzyme.

The full length GMPase from Arabidopsis has been isolated since the filing of the instant specification. This sequence, NM_129535 (Town et al, 2002, GeneBank Accession No.

NM_129535) is shown below, aligned with T46645 (T46645 is shown in bold, bases that do not match with NM_129535 are shown in lower case):

T46645 vs NM_129535

ATTTTGCCAACGAACGTTCTTTCTTCTTAATCACAGCNCAGCCTGACGCAACC
GCCTATCATTTTGCCAACGAACGTTCTTTCTTCTTAATCACAGCTCAGCCTGACGCAACC 60

GCTCAGGCTGATCTNTTCCAATTTACAGCCATTTCCCAGCTCAGATCTCTGATCCGGTGA
GCTCAGGCTGATCTCTTCCAATTTACAGCCATTTCCCAGCTCAGATCTCTGATCCGGTGA 120

GATCTCTCTCAAGGAAAAGGAGTTAGAGCATCATCAAGATGAAGGCACTCATTCTTGTTG
GATCTCTCTCAAGGAAAAGGAGTTAGAGCATCATCAAGATGAAGGCACTCATTCTTGTTG 180
MetLysAlaLeuIleLeuValG

CGAGGCTTCGGCACTCGCTTGAGACATTGACTCTCAGTTTCCCAAAGCCCCTTGTTGATT
GAGGCTTCGGCACTCGCTTGAGACCATTGACTCTCAGTTTCCCAAAGCCCCTTGTTGATT 240
lyGlyPheGlyThrArgLeuArgProLeuThrLeuSerPheProLysProLeuValAspP

TTNCTAATAAACCCATGATCCTTCATCAGATAGAGGCTCTTAAGGCAGTTGGAGTTGATG
TTGCTAATAAACCCATGATCCTTCATCAGATAGAGGCTCTTAAGGCAGTTGGAGTTGATG 300
heAlaAsnLysProMetIleLeuHisGlnIleGluAlaLeuLysAlaValGlyValAspG

AAGTGGTTTTGGCCATCAATTATCAGCCAGAGGTGATGCTGAACTTCTTGAAGGACTTTN
AAGTGGTTTTGGCCATCAATTATCAGCCAGAGGTGATGCTGAACTTCTTGAAGGACTTTG 360
luValValLeuAlaIleAsnTyrGlnProGluValMetLeuAsnPheLeuLysAspPheG

AGaccaaGCTGGaaaTCaaaaTCacttGctcacaAgagccgagcnactAggTaccgctg
TAGGTACCGCTGGTCCTCTGGCTCTAGCGAGAGACAAATTGCTTGATGGATCTGGAGAGC 420
euGlyThrAlaGlyProLeuAlaLeuAlaArgAspLysLeuLeuAspGlySerGlyGluP

gtcctTggtttannggGgnGcAAATtgnttTatggacCTgngngccctttttGttttaaaa
CCTTCTTTAGACCAAGCTGGAAATCAAAATCACTTGCTCACAAGAGACCGAGCCACGTTC 480
roPhePheluThrLysLeuGluIleLysIleThrCysSerGlnGluThrGluProLValL

gnnAtgantAaGgggncccnntaaAnaanCTTnggGtt
TTAACAGTGATGTGATTAGTGAGTACCCTCTTAAAGAAATGCTTGAGTTTCACAAATCTC 540
euAsnSerAspValIleSerGluTyrProLeuLysGluMetLeuGluPheHisLysSerH

AACGGTGGGGAAGCCTCCATAATGGTAACAAAGGTGGATGAACCGTCGAAATATGGAGTG 600
isGlyGlyGluAlaSerIleMetValThrLysValAspGluProSerLysTyrGlyValV

GTTGTTATGGAAGAAGCACTGGAAGAGTGGAGAAGTTTGTGGAAAAGCCAAAACTGTATG 660
alValMetGluGluSerThrGlyArgValGluLysPheValGluLysProLysLeuTyrV

TAGGTAACAAGATCAACGCTGGGATTTATCTTCTGAACCCATCTGTTCTTGATAAGATTG 720
alGlyAsnLysIleAsnAlaGlyIleTyrLeuLeuAsnProSerValLeuAspLysIleG

AGCTAAGACCGACTTCAATCGAAAAAGAGACTTTCCCTAAGATTGCAGCAGCGCAAGGGC 780
luLeuArgProThrSerIleGluLysGluThrPheProLysIleAlaAlaAlaGlnGlyL

TCTATGCTATGGTGCTACCAGGGTTTTGGATGGACATTGGGCAACCCCGTGACTACATAA 840
euTyrAlaMetValLeuProGlyPheGlnMetAspIleGlyGlnProArgAspTyrIleT

CGGGTTTGAGACTCTACTTAGACTCCCTTAGGAAGAAATCTCCTGCCAAATTAACCAGTG 900
hrGlyLeuArgLeuTyrLeuAspSerLeuArgLysLysSerProAlaLysLeuThrSerG

GGCCACACATAGTTGGGAATGTTCTTGTTGACGAAACCGCTACAATTGGGGAAGGATGTT 960
lyProHisIleValGlyAsnValLeuValAspGluThrAlaThrIleGlyGluGlyCysL

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TGATTGGACCAGACGTTGCCATTGGTCCAGGCTGCATTGTTGAGTCAGGAGTCAGACTCT     1020
euIleGlyProAspValAlaIleGlyProGlyCysIleValGluSerGlyValArgLeuS

CCCGATGCACGGTCATGCGTGGAGTCCGCATCAAGAAGCATGCGTGTATCTCGAGCAGTA     1080
erArgCysThrValMetArgGlyValArgIleLysLysHisAlaCysIleSerSerSerI

TCATCGGGTGGCACTCAACGGTTGGTCAATGGGCCAGGATCGAGAACATGACGATCCTCG     1140
leIleGlyGlnHisSerThrValGlyGlnGlnAlaArgIleGluAsnMetThrIleLeuG

GTGAGGATGTTCATGTGAGCGATGAGATCTATAGCAATGGAGGAGTTGTTTTGCCACACA     1200
lyGluAspValHisValSerAspGluIleTyrSerAsnGlyGlyValValLeuProHisL

AGGAGATCAAATCAAACATCTTGAAGCCAGAGATAGTGATGTGAAAATGAGATATTATAT     1260
ysGluIleLysSerAsnIleLeuLysProGluIleValMet

GTGCAACTTTTTTTTTTTTTTTGTGTCCTTTCTTCAACTTTGAAATCGCTTTCGTAATT     1320
CTTAATGGCTTTTGAATAAGCATCAATCAAAACGCTGTATATCTTGTTAGGGTCGTTTGC     1380
TGTTTTGTCTCTTTTTTTGTTTTGTAATTTATAAAAAAATTTATTCTCATTTTATGTGAG     1440
ATACTTTTGAATATTCATTAATTATAAAGCTTTTTTTTTGTGAAGTAA                 1488
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It is clear from this alignment that T46645 does not encode the full-length GMPase sequence. Furthermore, sequence differences mean that even within the portion of T46645 and NM_129535 that overlap, T46645 encodes a protein with a different amino acid sequence that does NM_129535. Thus, this sequence could not be used to produce plants with increased levels of vitamin C.

What Applicant transformed into the *vtc1* mutant was vector gVTC1-GPTV, which comprises a 3.4 kb DNA from the VTC1 locus (specification, pg 14, lines 1-6); this DNA is more than 6 times longer than the 510 nucleotides of T46645 and presumably comprises the full length GMPase as shown in NM_129535.

Davey et al (1999, Plant Physiol. 121:535-543) teach that there is more than one pathway for vitamin C synthesis in Arabidopsis; all of these pathways use L-galactone-1,4-lactone as the precursor before L-ascorbic acid, but they each produce L-galactone-1,4-lactone from very different precursors (Figure 4). Gatzek et al (2002, Plant J. 30:541-553) expressed in plants a nucleic acid encoding L-galactose dehydrogenase, which is the second-to-last enzyme in the vitamin C biosynthesis pathway shown in the instant Figure 1. Although the enzyme level was

increased 3.5 fold, there was no increase in vitamin C concentration in leaves (see abstract). In contrast, Agius et al (2003, Nature Biotechnol. 21:177-181) teach that expression of a nucleic acid encoding D-galacturonate reductase, an enzyme in one of the other pathways, did result in increased levels of vitamin C relative to wild-type plants. These results suggest that expression of a nucleic acid encoding any of the enzymes before galactono-1,4-lactone dehydrogenase the vitamin C biosynthesis pathway shown in the instant Figure 1, including phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase, would not increase vitamin C levels relative to those in wild-type plants.

Thus, it would not be possible to achieve an increased vitamin C concentration in plants by transformation with a nucleic acid encoding phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase, and transformation with a nucleic acids encoding one of those enzymes would not result in increased vitamin C content or increased resistance to drought, cold, UV radiation, air pollution, salts, heavy metals and/or reactive oxygen species.

Applicant is invited to submit a Declaration showing that plants transformed with a nucleic acid encoding phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase behave differently than plants transformed other nucleic acids encoding the enzymes before galactono-1,4-lactone dehydrogenase in the vitamin C pathway of in the instant Figure 1 and have increased levels of vitamin C and increased stress resistance relative to wild-type plants. This Declaration, however, will not enable the nucleic acid encoding GMPase from Arabidopsis. Only a deposit of gVTC1-GPTV, as below, will do that.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty

and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for increasing the endogenous level of vitamin C and resistance to environmental stresses in a plant by expression by of a nucleic acid encoding phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase.

Applicant and the Declaration urge that the specification provides ample guidance for the full-length gene encoding GMPase, based on T46645; thus, no experimentation would be required to obtain the clone (response pg 7-8 and Declaration ¶14).

This is not found persuasive because, as discussed above, T46645 is not a full-length clone of a sequence encoding a full-length GMPase.

Applicant urges that a deposit of full-length clone T517 is unnecessary because the sequence of the cDNA encoding the Arabidopsis GMPase is available from GenBank #T46645 (response pg 8).

This is not found persuasive because, as discussed above, T46645 is not a full-length clone of a sequence encoding a full-length GMPase.

Applicant and the Declaration urge that the specification provides ample guidance for wild-type plants transformed with the GMPase gene and method of making stress-resistant plants by transformation with that gene. Applicant and the Declaration urge that the specification provides examples in which plants were transformed with the full-length clone encoding GMPase and which exhibited increased vitamin C levels (response pg 8 and Declaration ¶17 - note there are no paragraphs 15-16 in the Declaration).

This is not found persuasive. Applicant on pg 16-17 transformed a mutant *vtc1-1* plant with a GMPase clone, effectively converting a mutant plant into a wild-type plant. This procedure is called complementation and the experiment merely showed that the clone was from the vtc1 gene. If the experiment had been unsuccessful, it would have shown the cDNA was not from the vtc1 gene. Applicant did not transform a wild-type plant with the GMPase cDNA clone to show that the plants so produced have increased levels of vitamin C relative to wild-type plants.

Applicant and the Declaration urge that Bauw et al teach that plants transformed with a nucleic acid encoding galactono-1,4-lactone dehydrogenase have increased vitamin C levels and increased stress resistance (response pg 9 and Declaration ¶18).

This is not found persuasive. Galactono-1,4-lactone dehydrogenase is the last enzyme in all the pathways for vitamin C synthesis, as discussed above, and transformation of a plant with a nucleic acid encoding galactono-1,4-lactone dehydrogenase would thus be expected to increase vitamin C levels in a plant relative to a wild-type plant.

Applicant urges that a prior Office Action asserted that plants transformed with a nucleic acid encoding phosphomannose isomerase, as taught by Trulson et al, would inherently have increased vitamin C levels and increased stress resistance (response pg 9).

This is not found persuasive because, in light of the teachings of Gatzek et al, plants transformed with a nucleic acid encoding phosphomannose isomerase would not inherently have increased vitamin C levels and increased stress resistance.

Applicant urges that both teachings in the art and Applicant's specification teach that a wide variety of plants can be transformed with a gene encoding an enzyme in the vitamin C biosynthetic pathway, thereby increasing the levels of vitamin C and stress resistance of the plants (response pg 9).

This is not found persuasive because, as discussed above, transformation of a plant with a nucleic acid encoding any of the enzymes before galactono-1,4-lactone dehydrogenase the vitamin C biosynthesis pathway shown in the instant Figure 1, including phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase, would not increase vitamin C levels relative to those in wild-type plants.

Applicant and the Declaration urge that Applicant has subsequently identified another gene in the vitamin C biosynthetic pathway, VTC4, using methods identical to those in the present specification; thus the specification provides enablement for the claimed invention (response pg 9-10 and Declaration ¶19).

This is not found persuasive. The instant claims are not drawn to a method of increasing vitamin C levels and increasing stress resistance in a plant by transformed with the VTC4 gene and plants thereby obtained.

Applicant and the Declaration urge that any unpredictability associated with the expression of genes in plants has been overcome by Applicant's transformation of the GMPAse gene into plants to produce plants with increased levels of vitamin C relative to progenitor plants (response pg 10 and Declaration ¶20).

This is not found persuasive. Applicant on pg 16-17 transformed a mutant *vtc1-1* plant with a GMPase clone, effectively converting a mutant plant into a wild-type plant. Applicant did not transform a wild-type plant with the GMPase cDNA clone to show that the plants so produced have increased levels of vitamin C relative to wild-type plants. Furthermore, Applicant did not use a clone where the only GMPase sequence was that of T46645.

7. Claims 1-22 and 24-26 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 17 June 2003. Applicant's arguments filed 17 September 2003 have been fully considered but they are not persuasive.

Applicant and the Declaration urge that many of the genes encoding GMPase, including Arabidopsis, and the other enzymes in the vitamin C pathway are known in the art (response pg 12 and Declaration ¶22).

This is not found persuasive because the coding sequence of full-length Arabidopsis GMPase gene is not known in the prior art. Furhtermore, it is not clear that any plant genes encoding phosphoglucose isomerase, phosphomannomutase. Lastly, even if some genes encoding phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose

epimerase wree known, such sequences do not describe the full scope of genes encoding phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase

Applicant and the Declaration urge that Figure 1 and the specification on pg 4 disclose the enzymes in the vitamin C pathway (response pg 12 and Declaration ¶23).

This is not found persuasive. Disclosure of a list of enzyme names does not describe the structural features, that is, the sequence, of the nucleic acids that encode such enzymes.

Applicant and the Declaration urge that based on the examples and results disclosed in the application, one of skill in the art would know that they were in possession of the GMPase gene and plants transformed with it (response pg 12 and Declaration ¶24).

This is not found persuasive because, as discussed above, the coding sequence of full-length Arabidopsis GMPase gene is not described in the specification.

8. Claims 1-8, 10, 16-22 and 24-26 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 17 June 2003. Applicant's arguments and the Declaration of Dr. Patricia Conklin, both filed 17 September 2003, have been fully considered but they are not persuasive.

Claim 1 remains indefinite in its recitation of "plant Vitamin C biosynthesis pathway." It is not clear if this means the nucleic acid is derived from plants or if the nucleic acid encodes any pathway enzyme that can function in plants.

Applicant and the Declaration urge that the enzymes encompassed by the claims are described in Figure 1 and the source of nucleic acids that encode these enzyme is not relevant since the claims have no limitation as to source (response pg 13 and Declaration ¶11).

This is not found persuasive because an enzyme in a plant biosynthetic pathway would have to be one from a plant, as plants do not have bacterial, fungal or animal enzymes. Additionally, plants have more than one possible vitamin C pathway (Davey et al, 1999, Plant Physiol. 121:535-543).

Claims 2 and 10 are indefinite in their recitation of "said plant, or portion thereof, is a dicot". Is Applicant saying that only a portion of the plant is a dicot? What is the rest of the plant?

Applicant and the Declaration urge that one of ordinary skill in the art would understand that the claims encompass plant cells, protoplasts, callus, tissue cultures obtained from dicots and whole plants that are dicots (response pg 13-14 and Declaration ¶12).

This is not found persuasive because the claim as worded is confusing because it states that the portion of the plant is a dicot, making one wonder what the rest of the plant is. It is suggested that the claim be amended to delete ", or portion thereof,". This would inherently mean that the portion is from a dicot.

The term "increasing" in claim 16 is a relative term that renders the claim indefinite. The term "increasing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the level of vitamin C be compared to that of a wild-type plant.

Applicant and the Declaration urge that one of ordinary skill in the art would understand the meaning of the term and apply its plain ordinary meaning; thus there is no need to define the term as everyone would understand the plants have increased vitamin C relative to untransformed plants (response pg 14 and Declaration ¶13).

This is not found persuasive because relative terms render claims indefinite. It is noted that comparisons to untransformed plants are already made for the plants of claims 6-7 and 13-14 and for method claims 20-21, both of which are dependent upon claim 16. Claims 20-21 fail to further limit claim 16, as discussed above.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1-22 and 24-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 and 27 of copending Application No. 09/909,600. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of increasing the endogenous level of vitamin C in a plant and increasing the resistance to environmental stress by expression of

phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase, and plants thereby obtained, as claimed in the copending application, is identical to a method of increasing the endogenous level of vitamin C in a plant and increasing the resistance to environmental stress by expression of phosphoglucose isomerase, phosphomannomutase, GMPase, or GDP-mannose epimerase, and plants thereby obtained, as claimed in the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
November 24, 2003

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600